



(1) Publication number:

0 520 486 A2

## (2) EUROPEAN PATENT APPLICATION

(21) Application number: **92110804.9** 

(51) Int. Cl.5: **A61M** 1/36

2 Date of filing: 26.06.92

3 Priority: 28.06.91 JP 158775/91

43 Date of publication of application: 30.12.92 Bulletin 92/53

② Designated Contracting States:
AT BE CH DE DK FR GB IT LI NL SE

Applicant: Sumitomo Electric Industries, Ltd. 5-33, Kitahama 4-chome, Chuo-ku Osaka 541(JP)
Applicant: Tachibana, Shunro 1-6-18, Kusagae
Chuo-ku Fukuoka-shi Fukuoka-ken(JP)

Inventor: Tachibana, Shunro 6-18, Kusagae 1-chome, Chuo-ku Fukuoka-shi, Fukuoka-ken(JP) Inventor: Sogawa, Ichiro, c/o Osaka Works of Sumitomo

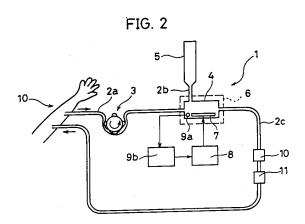
Electric Ind., Ltd., 1-3, Shimaya 1-chome Konohana-ku, Osaka(JP) Inventor: Tachibana, Katsuro

6-18, Kusagae 1-chome, Chuo-ku Fukuoka-shi, Fukuoka-ken(JP)

(4) Representative: Kirschner, Klaus Dieter et al Patentanwälte Herrmann-Trentepohl, Kirschner, Grosse, Bockhorni & Partner Forstenrieder Allee 59
W-8000 München 71(DE)

# (54) Blood processing for treating blood disease.

© Provided are a method and an apparatus which can make effective chemical treatment of a blood disease by applying a drug of a wider range with a smaller dose or lower concentration. Blood which is collected from a patient is fed from a tube (2a) into a chamber (4) by a pump (3). A drug is injected into the chamber (4) from a container (5), while ultrasonic waves are applied to the blood contained in the chamber (4) from an actuator (7). The blood treated with the drug and the ultrasonic waves is returned into the body of the patient through a tube (2c), while the same is monitored by sensors (10) and (11).



10

15

25

30

35

40

45

50

55

#### BACKGROUND OF THE INVENTION

#### Field of the Invention

The present invention relates to blood processing, and more particularly, it relates to a blood processing method and a blood processing apparatus for chemically treating a blood disease such as leukemia, and a method of treating a blood disease.

### Description of the Background Art

In order to chemically treat a blood disease such as leukemia, a remedy is directly administered into the body of the patient in general. For example, a patient who receives chemical treatment often gets an intravenous injection of a carcinostatic substance. When he suffers from leukemia, he receives administration of a toxic drug for attacking rapidly propagating leukocytic cells, or such a drug is administered in relatively high intravascular concentration for attaining a good effect. This often leads to various side reactions.

On the other hand, there has been developed a new chemical treatment method employing an apparatus called a photophoresis apparatus in treatment of a cutis T cell lymphadenoma (CTCL) ("Science" Japan Edition, October 1988, pp. 65 -73). As shown in Fig. 1, such a photophoresis apparatus 20 comprises a centrifugal separator 21 for separating blood into components, and is controlled by a microprocessor. In this apparatus, blood components contained in a bag 22a are fed through a transparent passage 23 of plastic, to be stored in another bag 22a. High-power ultraviolet lamps 24 are provided on both sides of the passage 23. The blood of a patient is separated into components by the centrifugal separator 21, so that blood plasma and leukocytes are contained in the bag 22a. The components thus contained in the bag 22a are mixed with a physiological salt solution which is contained in a bag 22c, and fed into the passage 23. The ultraviolet lamps 24 apply intense ultraviolet radiation A (UVA) to the liquid which is passed through the passage 23. The UV-irradiated components are mixed with other centrifugally separated components, and returned into the body of the patient.

The photophoresis apparatus has brought means for optically processing the blood or the blood components of a patient with a drug in the exterior. This has conceivably developed a way to chemical treatment for optically activating a drug and selectively applying the same to a target.

### SUMMARY OF THE INVENTION

The inventors have considered that it is necessary to study not only optical activation of a drug but also improvement of its action in a wider range. When a drug is optically activated, it may conceivably be necessary to take light transmittance of an object such as blood into consideration in order to attain sufficient activation, and hence treatment conditions may be restricted. Particularly in treatment of a blood disease, there has been required means which can make effective treatment even if various drugs to be administered are suppressed in concentration.

In order to satisfy such requirements, an object of the present invention is to provide a method and an apparatus which can make effective treatment by applying a wider range of a drug with a smaller dose or lower concentration, particularly in chemical treatment of a blood disease.

According to a first aspect of the present invention, provided is a blood processing apparatus which comprises a passage having an inlet and an outlet for passing blood therethrough, a pump for feeding the blood from the inlet toward the outlet of the passage, drug injection means for injecting a drug into the passage, and ultrasonic wave application means for applying ultrasonic waves to the blood which is mixed with the drug in the passage.

In the blood processing apparatus according to the present invention, the blood of a patient is supplied into the passage from the inlet, so that the same can be fed toward the outlet by the pump. In the passage, the blood is mixed with a drug by the drug injection means. The ultrasonic wave application means applies ultrasonic waves to the blood which is mixed with the drug. Thus, the blood of the patient is ultrasonic-treated with the drug, and then discharged from the outlet of the passage.

According to another aspect of the present invention, provided is a processing blood method. In this method, the blood of a patient is fed through a tubular structure, for example, at a prescribed flow rate. An effective dose of a drug is added to the blood in this structure. The drug can be maintained in constant concentration in the blood. Simultaneously with or following such addition of the drug, ultrasonic waves are applied to the blood. The blood treated with the ultrasonic waves is discharged from the structure, so that the same is introduced into the body of the patient.

According to the present invention, the ultrasonic-treated blood is preferably regularly monitored. Various sensors can be employed for this purpose.

After the ultrasonic treatment, the drug which is left in the blood can be preferably removed in order to suppress a side reaction caused on the patient. In this case, the blood is supplied to the patient after such removal of the drug.

According to still another aspect of the present invention, provided is a method of treating a blood disease. In this method, blood is first collected from a patient. Then, an effective dose of a drug is added to the blood. Simultaneously with or following such addition of the drug, ultrasonic waves are applied to the blood. The ultrasonic-treated blood is returned into the body of the patient.

This treatment method can be applied to leukemia, for example. In this case, a carcinostatic substance, for example, can be added to the collected blood, in order to attack malignant lymphocytic cells.

This treatment method can be carried out while the blood of the patient is circulated in the exterior by an external circulation system. In this case, the drug is continuously or intermittently added to the externally circulated blood. The blood containing the drug is treated with ultrasonic waves.

Also in this treatment method, the ultrasonic-treated blood is preferably monitored. Further, the drug which is added to the blood is preferably removed before the blood is returned into the body of the patient.

The foregoing and other objects, features, aspects and advantages of the present invention will become more apparent from the following detailed description of the present invention when taken in conjunction with the accompanying drawings.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a perspective view showing a conventional blood processing apparatus;

Fig. 2 is a typical diagram showing a concrete example of a blood processing apparatus according to the present invention; and

Fig. 3 is a perspective view showing an assembled state of the apparatus shown in Fig. 2.

### DESCRIPTION OF THE PREFERRED EMBODI-MENTS

Fig. 2 is a typical diagram showing a concrete example of an apparatus 1 which is applied to blood processing according to the present invention. In this blood processing apparatus 1, a tube 2a for introducing the blood of a patient 10 into the apparatus 1 is connected to a chamber 4. The tube 2a, which is made of vinyl chloride resin, polyethylene, silicone resin or the like, for example, is wound on a rotary head of a separately provided roller pump 3. Thus, the asintroduced blood is fed to the chamber 4 at a constant flow rate. On the other hand, the chamber 4, which is adapted to mix the blood with a drug and treat the same with ultrasonic waves, is provided with a container 5 for containing the drug through a tube 2b. The drug is

introduced into the chamber 4 at a constant flow rate by a separately provided pump (not shown). The chamber 4 can be kept warm by a heater 6 which is provided on its outer periphery. The chamber 4 is provided therein with an ultrasonic actuator 7, which is connected with a transmission circuit 8 provided in the exterior of the chamber 4. The ultrasonic actuator 7, which is capable of generating ultrasonic waves in a frequency range of 10 KHz to 10 MHz, for example, can be formed by an electrostrictive element or a magnetostrictive element. The chamber 4 is further provided therein with an ultrasonic power monitor sensor 9a for controlling the ultrasonic waves, which is electrically connected with an ultrasonic power monitor circuit 9b provided in the exterior of the chamber 4. The transmission circuit 8 is controlled by a signal which is detected by the sensor 9a and processed by the monitor circuit 9b, thereby controlling the output of the ultrasonic waves. A tube 2c is provided in the chamber 4 in a position opposite to the tube 2a, in order to discharge the fluid from the chamber 4. The tube 2c, which can be made of vinyl chloride resin, polyethylene or silicone resin similarly to the tube 2a, can be provided with a hemolysis sensor 10 and a bubble sensor 11. The hemolysis sensor 10 can be prepared from a member for detecting hemolysis by change of light transmittance, or the like. The state of the blood discharged from the tube 2c can be monitored by the sensors 10 and 11. If necessary, still another sensor can also be provided. The tube 2c can be used for returning the blood into the body of the patient 10. In the apparatus 1 having the aforementioned structure, the blood of the patient 10 is mixed with a proper dose of a drug and treated with ultrasonic waves in the chamber 4, and thereafter returned into the body of the patient 10. Thus, the apparatus 1 shown in Fig. 2 can be employed as an external circulation system, while the same can also be employed as an apparatus for processing separately collected blood.

The apparatus 1 typically illustrated in the aforementioned manner can be assembled as shown in Fig. 3, for example. In the apparatus shown in Fig. 3, a display 12 displays feed rates of the pump 3 and the pump (not shown) for supplying the drug into the container 5, the output of an ultrasonic unit 17, the temperature of the chamber 4, and data from the hemolysis sensor 10 and the bubble sensor 11. The feed rates, the output of the ultrasonic unit 17, the temperature of the chamber 4 and the like can be controlled by an operation panel 13. In relation to this apparatus, it is possible to provide another system for supplying another drug, thereby supplying a plurality of drugs into the chamber 4. Further, when the tube 2c for discharging the blood which has been processed in

55

30

40

45

5

15

20

25

30

35

40

50

55

6

the chamber 4 is provided with means, such as a filter, for example, for removing the drug, it is possible to remove only the drug from the blood, thereby effectively suppressing a side reaction. In addition, portions for passing the blood therethrough, such as the tubes 2a to 2c and the chamber 4, for example, can be formed by throw-away members. Further, outlets for taking the blood before and after processing can be formed on the tubes 2a and 2c connected to the chamber 4.

According to the inventive apparatus, as hereinabove described, the ultrasonic waves act on the blood components to improve the same in sensitivity to the drug. When the blood of a leukemic patient is processed, for example, the ultrasonic waves act on malignant lymphocytic cells to improve sensitivity to a carcinostatic substance. Consequently, it is possible to attain a preferable chemical treatment effect with a smaller dose of a drug. Since the drug is locally administered into the blood within the chamber, it is possible to attack the target with no waste. When the blood is returned into the body of the patient, the drug, which has been in effective concentration within the chamber, is so diluted that its toxicity is reduced. When the drug is removed from the blood by some means as hereinabove described, it is possible to maintain intravascular concentration of the drug at a lower value all over the body of the patient. Thus, it is possible to remarkably reduce a side reaction of the drug.

As hereinabove described, the present invention is adapted to mix blood with a drug and treat the same with ultrasonic waves, thereby improving the effect of the drug, particularly that for a blood disease, over an extremely wide range. According to the present invention, it is possible to bring a synergistic chemical treatment effect by the ultrasonic waves and the drug. According to the present invention, further, it is possible to effectively apply the drug with a small dose or small intravascular concentration, thereby reducing a side reaction. Thus, the present invention is extremely effectively applied to chemical treatment of a blood disease such as leukemia, autoimmune disease such as AIDS, sepsis and collagen disease, in particular.

Although the present invention has been described and illustrated in detail, it is clearly understood that the same is by way of illustration and example only and is not to be taken by way of limitation, the spirit and scope of the present invention being limited only by the terms of the appended claims.

### Claims

 An apparatus for blood processing, comprising: a passage having an inlet and an outlet for passing blood therethrough;

a pump for feeding said blood from said inlet toward said outlet in said passage;

drug injection means for injecting a drug into said passage; and

ultrasonic wave application means for applying ultrasonic waves to said blood being mixed with said drug in said passage.

- 2. An apparatus in accordance with claim 1, further comprising a sensor for monitoring said blood being discharged from said passage.
  - An apparatus in accordance with claim 1, further comprising removal means for removing said drug from said blood flowing in said passage after injection of said drug.
  - 4. An apparatus in accordance with claim 1, wherein said passage comprises:
    - a tube for introducing said blood, and
    - a chamber being connected with said tube for mixing said blood with said drug while applying ultrasonic waves therein.
  - An apparatus in accordance with claim 4, wherein an ultrasonic transmission element is provided in said chamber,

said ultrasonic transmission element being connected with a transmission circuit provided in the exterior of said chamber.

- An apparatus in accordance with claim 1, being applied to an external circulation system for treating a patient.
- 7. A method of blood processing, comprising:
  - a step of feeding blood into a prescribed passage at a prescribed rate;
  - a step of adding a drug to said blood flowing in said passage in a prescribed ratio;
  - a step of applying ultrasonic waves to said blood containing said drug in said passage; and
  - a step of discharging ultrasonic-treated said blood from said passage.
- **8.** A method in accordance with claim 7, further comprising a step of monitoring said blood being discharged from said passage.
- 9. A method in accordance with claim 7, further comprising a step of removing said drug being left in said blood before discharge of said blood from said passage upon addition of said drug.
- 10. A method of treating a patient having a blood

10

15

25

30

disease, said method comprising:

- a step of collecting blood from said patient;
- a step of adding a drug to collected said blood;
- a step of applying ultrasonic waves to said blood containing said drug; and
- a step of returning ultrasonic-treated said blood into the body of said patient.
- 11. A method in accordance with claim 10, wherein a prescribed volume of said blood being continuously collected from said patient is treated with a prescribed dose of said drug and ultrasonic waves, to be thereafter continuously returned into the body of said patient.
- **12.** A method in accordance with claim 10, further comprising a step of removing said drug being left in said blood before ultrasonic-treated said blood is returned into the body of said patient.
- **13.** A method in accordance with claim 10, further comprising a step of monitoring ultrasonic-treated said blood.
- **14.** A method in accordance with claim 10, wherein said blood disease is leukemia.
- **15.** A method in accordance with claim 10, wherein said drug includes a carcinostatic substance.
- **16.** A method in accordance with claim 14, wherein said drug includes a carcinostatic substance.

40

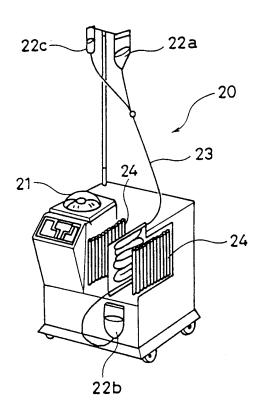
35

45

50

55

FIG. 1





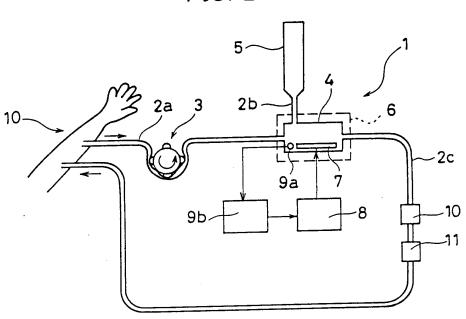


FIG. 3

